phenomenon and may not lead initially to enlargement of the liver.

Given the worsening nature of the patient's ascites after vitamin A intake was discontinued, a way was sought to maximize the removal of the vitamin A by increasing the RBP levels. Nutritional supplementation was given to provide an adequate protein intake. A trial of prednisone was used to increase the mobilization of hepatic vitamin A by increasing the release of RBP from the liver.[1,12]

In summary, this case report describes an unusual presentation of chronic vitamin A intoxication. It suggests that children with malnutrition may be at a greater risk for intoxication because of impaired RBP production and can present with normal vitamin A levels. Determining the retinol-binding protein level is vital in the diagnosis and helpful in deciding the management. Last, although most patients' symptoms resolve simply by withdrawing the vitamin A supplementation and providing good nutrition, a trial of steroids may be considered in patients with persistent clinical symptoms.

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Dysgonic Fermenter-2 Infections

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DOG BITES have been known to cause dangerous sepsis. The most commonly known bacterium is *Pasteurella multocida.* A search of the English language literature was made using MEDLINE 1977-1986 files. Since 1976 there have been multiple reports of dysgonic fermenter (DF-2) infections, many of them following dog bites or casual exposure to dogs. Dysgonic (Greek *dys,* "difficult," plus *gonikos,* "seed, offspring") fermenters are fastidious gram-negative rods easily missed by routine culture media. They are found in the oropharynx of some dogs. Patients with the worst prognosis tend to have splenectomies, alcoholism, or chronic obstructive pulmonary disease.

ABBREVIATIONS USED IN TEXT
DF-2 = dysgonic fermenter
HIA = heart infusion agar

There have been 42 previously documented cases of DF-2 infections (one of them presumptive). The clinical spectrum has ranged from self-limited disease to fatal sepsis. The actual incidence is predictably higher than reported because of the difficulties with culture. DF-2 needs enriched media for growth and fermentation. Previous strains have reportedly been susceptible to penicillin. This is the first case description of penicillin resistance with DF-2.

Report of a Case

The patient, a 65-year-old man, had suffered from chronic obstructive pulmonary disease, nephrolithiasis, and hypertension. He was bitten on the left third finger by a dog on March 9, 1986. The following day he described shaking chills and on March 11 had temperatures up to 40°C (104°F). He was admitted to hospital the next day with a blood pressure of 85/70 mm of mercury, confusion, and fecal incontinence. The skin was acrocyanotic with ecchymotic, purpuric, and petechial lesions involving the extremities, face, and periumbilical area. Gangrene developed on the bitten finger without evidence of osteomyelitis. There were no mucosal or retinal lesions. The lungs were clear, and the heart had a II/VI systolic murmur at the apex and aortic valve area. The abdomen was soft without tenderness or organomegaly. There was no costovertebral angle tenderness despite complaints of back pain.

Initially the prothrombin time was 22 seconds, partial thromboplastin time 100 seconds, platelet count 14×10^9 per liter (14,000 per μl), hematocrit 0.39 (38.7%), and hemoglobin 8.4 mmol per liter (13.5 grams per dl). The leukocyte count was 6.6×10^9 per liter (6,600 per μl), with 0.54 (54%) neutrophils, 0.32 (32%) bands, 0.07 (7%) lymphocytes, and 0.06 (6%) metamyelocytes. Serum electrolyte values were normal except for a bicarbonate of 12 mmol per liter (12 mEq per liter). The blood urea nitrogen level was 22.1 mmol per liter (62 mg per dl) and the serum creatinine level 475 μmol per liter (4.2 mg per dl).

The patient was treated with a regimen of penicillin G benzathine, 12 million units per day, and ceftizoxime sodium, 6 grams per day, given intravenously. He became more alert, and his hemodynamic indicators improved after fluid replacement and correction of the metabolic acidosis.

On March 15, he had a respiratory arrest requiring assisted ventilation. His condition continued to deteriorate, and he died on March 18, nine days after the dog bite. The main autopsy findings included a hemorrhagic spleen, congestion of the entire mucosa of the small and large intestines, and mucosal edema and hemorrhage of the major bronchi. The thyroid, adrenal, and pituitary glands were edematous.

All the blood cultures from admission became positive in 48 hours (March 14), with a fastidious gram-negative rod by the Bactec 6A automated system (Johnstons Laboratories, Townson, Md). A preliminary identification of DF-2 was made on March 17, 1986, and was later corroborated by the State of California Microbial Diseases Laboratory. Its growth

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requirements and biochemical pattern (Table 1) are similar to the previously reported DF-2. The organism does not grow on MacConkey agar or unsupplemented broth. Growth occurred in enriched chocolate agar (gonococcal agar, hemoglobin, reagents for *Neisseria* and *Hemophilus influenzae*) and blood agar (tryptic soy agar plus 5% sheep erythrocytes), both supplied by Remel Laboratories, Lenexa, Kansas. Repeat cultures after antibiotic therapy was begun remained negative.

The antibiotic susceptibility pattern is different from that in previously reported cases of DF-2 infection. Because of poor growth on routine media, the broth-disk elution method for anaerobic bacteria described by Wilkins and Thiel[1] was used. This patient's bacteria were susceptible to chloramphenicol (12 μg per ml), ceftizoxime (18 μg per ml), and metronidazole (16 μg per ml), but not to penicillin (2 units per ml), clindamycin (1.6 μg per ml), or erythromycin (3 μg per ml).

TABLE 1.—*Characteristics of Bacteria in Patient With Dysgonic Fermenter-2 Infection*

Morphology	Long, thin, spindled gram-negative rod
Catalase	+
Oxidase	+
Growth	
MacConkey agar	–
SS agar	–
Blood and chocolate agar	
25°C (days)	+ (2-4)
35°C (days)	+ (2)
42°C	–
Aerobically	+
Carbon dioxide 5%	+
Fermentation	
Phenol red broth + rabbit serum	
Glucose (days)	A (2)
Lactose (days)	A (3-5)
Maltose (days)	A (3-5)
Triple sugar iron	
Slant/aerobic	Aw
Butt/anaerobic	–
Hydrogen sulfide	–
Lead acetate	+

A = acid; Aw = acid, weak reaction

Discussion

The first report of a case of DF-2 infection was published in 1976 by Bobo and Newton.[2] The following year 17 cases, including that of Bobo and Newton, were reviewed by Butler and co-workers.[3] An additional 25 cases have been reported in the English literature.[4-26]

Most reviews of animal bites fail to recognize DF-2 as a pathogen. In a previous evaluation of canine oral flora, DF-2 was not detected.[27] In two reported cases DF-2 was recovered from the dogs' gingivae.[8,26]

The clinical presentations of documented cases include self-limited infections without the need of antibiotics,[9] cellulitis, gangrene, blepharitis,[25] arthritis, endocarditis[15] without fevers,[10] meningitis,[2,12,26] brain abscess,[16] disseminated intravascular coagulation, the Waterhouse-Friderichsen syndrome,[11] myocardial infarction,[23] and cardiopulmonary arrest.

Of the 43 cases, 24 (56%) were directly related to dog bites and others were associated with dogs. An underlying disease was present in 33 patients (77%). Splenectomy was noted in 17 patients (40%) and alcoholism in 10 (23%).

The overall mortality is 12/43 (28%). Nine of the deaths (9/12, or 75%) occurred in patients with some underlying disease. Conversely, 24 of 33 patients (73%) with underlying illness survived. Three of ten patients (30%) without underlying illness died. In four of ten patients (40%) who died, smears of their peripheral blood or buffy coats showed bacteria. There is no apparent element that correlates with the prognosis. It remains to be proved if the fatal cases are due to penicillin resistance or to a more virulent strain of DF-2.

The optimal culture medium for DF-2 has not been determined. The use of enriched chocolate and blood agar facilitated growth of the strain reported here. Fermentation reactions were possible by adding rabbit serum to the broth (Table 1). Different blood culture media have been used to recover DF-2. These include Bactec 6A, 6B aerobic bottles, 7C anaerobic bottles, trypticase-soy with sodium polyanethol sulfonate, supplemented peptone, and glucose broths. Subculture media have included heart infusion agar (HIA) with 5% rabbit blood in CO_2, trypticase-soy agar with 5% sheep blood, and HIA with 5% sheep blood.[28,29]

Penicillin has been described as the drug of choice, but, as with this patient, one must be aware of resistant strains that until now had not been described. The routine methods for antibiotic susceptibility tests—Kirby-Bauer, minimum inhibitory concentration with Mueller-Hinton broth, and so forth—are standardized for rapidly growing aerobic or facultative organisms. Slow-growing bacteria like DF-2 require modified techniques that allow adequate growth of the organism to detect any effect by the antibiotic being tested. The original strains of DF-2 described by Butler and associates[3] were tested by an agar dilution method using a special medium (Schaedler's). In most of the subsequent reports on DF-2, the authors failed to do or to report their susceptibility tests, sometimes only quoting the previous results of Butler and colleagues. Many community hospitals are not properly staffed or familiar with the technique of diluting agar for fastidious bacteria.

Broth-disk elution tests, such as Wilkins-Thiel's, are easier to do, are reproducible, and are more acceptable to laboratories with limited resources. Antibiotic disk(s) are diluted with broth in individual tubes. For penicillin, a 10-unit disk is diluted with 5 ml of medium, giving a penicillin concentration of 2 units per ml. One drop of bacterial inoculum is added to each tube containing antibiotic and to a control tube without antibiotic. The tubes are incubated and their turbidity is compared with the control tube. Susceptibility can be defined as the absence of turbidity. Reports are given as either susceptible or resistant to the given concentration of antibiotic tested.

Using penicillin alone might not be adequate therapy for sepsis following a dog bite. Administering a second antibiotic active against *Staphylococcus* and other gram-negative bacteria is appropriate while awaiting susceptibility studies. A reasonable regimen to treat a suspected DF-2 infection would be penicillin plus a third-generation cephalosporin like cefotaxime or ceftizoxime while awaiting bacteriologic reports. It would be difficult to justify the use of a first-generation cephalosporin as the main therapy for DF-2, considering its clinical failure with *P multocida*, the lack of central nervous system penetration, and the possible diagnoses listed below.

When a patient presents with petechiae, purpura, and ec-

chymosis, the differential diagnosis includes meningococcemia, Rocky Mountain spotted fever, and sepsis in asplenic and immune-compromised patients. The history of a dog bite should suggest the possibility of *P multocida* and DF-2 infections. Penicillin appears to be the drug of choice for DF-2 infections, but susceptibility tests should be done on all clinical organisms for the possibility of a resistant strain. The best alternative for patients who are either allergic to penicillin or who have penicillin-resistant infections is not known.

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